

Accuracy of intra-operative frozen section in the diagnosis of ovarian tumours

Arikan Ilker,¹ Barut Aykut,² Harma Muge,³ Harma Mehmet Ibrahim,⁴ Ozmen Bayar Ulku,⁵ Gezer Sener,⁶ Sun Suna⁷

Department of Gynecology and Obstetrics, Faculty of Medicine, Zonguldak Karaelmas University,^{1-5,7}

Obstetrics and Gynecology Clinic, Zonguldak Maternity Hospital,⁶ Zonguldak, Turkey.

Abstract

Objectives: To compare frozen-section results with definitive histopathological results of ovarian tumours diagnosed intra operatively at the Zonguldak Maternity Hospital, Zonguldak, Turkey.

Methods: The definitive histopathological results of 278 patients who underwent surgery between January 2002 and December 2008 for ovarian masses and on whom frozen sectioning was performed were evaluated retrospectively. After exclusion of 12 patients for whom a definitive result could not be obtained from frozen sections, the results of 266 patients' frozen sections were compared with those from permanent sections.

Results: Data of 266 patients was analyzed. The results of frozen sections were 235 (88.3%) benign, 11 (4.2%) borderline and 20 (7.5%) malignant. The sensitivity was 100% for the benign tumours, 77.8% for the borderline tumours and 71.4% for the malignant tumours. The specificity of frozen section was 83.8%, 98.4% and 100% for the benign, borderline and malignant tumours, respectively.

Conclusions: Frozen sections have adequate sensitivity and specificity at the Zonguldak Maternity Hospital, Turkey, and can be safely used to guide the intraoperative management of ovarian masses. False-positive and -negative ratios are low.

Keywords: Frozen section, Accuracy, Ovarian tumour, Intra-operative, Tumours, Zonguldak (JPMA 61:856; 2011).

Introduction

Discrimination of benign and malignant tumours during surgery in gynaecologic patients with adnexal masses is important for the management of the patient.^{1,2} Intra-operative frozen-section analysis gives information about the characteristics of masses.³⁻⁵ The results of the frozen examination determine the course of surgery.⁶⁻⁸ When malignant frozen-section results are obtained, the surgical field widens and staging is performed; this may involve total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, omentectomy, appendectomy, or multiple peritoneal biopsies.⁹ Benign or borderline frozen-section results limit the surgery to oophorectomy or cystectomy. Particularly for young patients, the diagnostic accuracy of frozen-section results is critical for fertility-conserving surgeries.^{10,11} The consequences of overdiagnosis may include unnecessary surgical intervention and increased morbidity and mortality. Alternatively, underdiagnosis is associated with secondary operations and tumoural spread.¹² This study aimed to evaluate the diagnostic concordance between the results of frozen section and those of paraffin block.

Materials and Methods

In this study, we retrospectively evaluated the definitive histopathological results of 278 patients who underwent surgery between January 2002 and December

2008 at Zonguldak Karaelmas University, Faculty of Medicine, Department of Obstetrics and Gynaecology for ovarian masses and on whom frozen section was performed. Twelve patients (4.3%) for whom a definitive result was not obtained from frozen sections were excluded from the study, and the remaining 266 patients' results were analysed. Each specimen collected from the operation site was transferred to the pathology unit with the patient's clinical details as soon as possible. The size and the presence of surface irregularities and vegetations were then macroscopically evaluated. Two to five samples taken from suspicious areas were frozen, cut into 5- μ m sections, and stained with haematoxylin and eosin. Both frozen and paraffin sections were examined by expert pathologists. The results were classified into three groups: benign, malignant, and borderline. Then, the results of frozen sections and paraffin blocks were compared. False-positive (malignant or borderline frozen result, but benign paraffin-block result) and false-negative (benign frozen result, but malignant or borderline paraffin-block result) results were examined. Cases with borderline frozen results and malignant paraffin-block results or with malignant frozen results and borderline paraffin-block results were also evaluated. Descriptive statistics were employed.

Statistical analyses were carried out by SPSS for Windows 11.0 (SPSS Inc; Chicago, III). Sensitivity, specificity, positive predictive values, and negative predictive values, of each group (benign, borderline and malignant) were assessed.

Results

In this study, frozen-section examinations of tumours from 266 patients were retrospectively reviewed. The mean age of the patients whose frozen sections were examined was 42.5 ± 13.5 years. The results of definitive histopathological diagnosis of all tumours are presented in Table-1.

Among the frozen-section results, 235 (88.3%) were benign, 11 (4.2%) were borderline, and 20 (7.5%) were malignant (Table 2). Of the definitive paraffin block results, 229 (86%) were benign, nine (3.4%) were borderline, and 28 (10.5%) were malignant (Table-2). In 256 of the 266 frozen sections, frozen-section results gave the same diagnosis as did results of the paraffin blocks. In 10 cases, the results were discordant. The accuracy rate was determined to be 96.2%.

There were two cases with benign frozen but borderline paraffin-block results; four cases had benign frozen but malignant paraffin-block results; and four cases showed

Table-1: The distribution of definitive histopathological diagnosis of all ovarian tumors.

Histopathological diagnosis		n	%
Benign	Functional cyst	229	100
	Mature cystic teratoma	117	51.1
	Mucinous cystadenoma	22	9.6
	Serous cystadenoma	24	10.5
	Endometrioma	18	7.9
	Fibrothecoma	35	15.3
	Serous cystadenofibroma	7	3.1
	Serous cystadenofibroma	5	2.1
	Benign Brenner tumour	1	0.4
Borderline		9	100
Malignant		28	100
	Epithelial Ovarian Tumour	16	57.1
	Germ Cell Tumour	10	35.7
	Other	2	7.2

Table-2: The results of frozen and paraffin sections in various categories of ovarian neoplasms (n=266).

Frozen Diagnosis	Final Diagnosis (Paraffin)		
	Benign	Borderline	Malignant
Benign (n=235)	229	2	4
Borderline (n=11)	0	7	4
Malignant (n=20)	0	0	20
Total (n=266)	229	9	28

Table-3: Sensitivity, specificity, PPV, and NPV of frozen sections (%).

	Benign	Borderline	Malignant
Sensitivity	100	77.8	71.4
Specificity	83.8	98.4	100
PPV	97.4	63.6	100
NPV	100	99.2	96.7

PPV, Positive predictive value; NPV, Negative predictive value.

borderline frozen but malignant paraffin-block results.

Table-3 shows the test performance (sensitivity, and specificity, and positive and negative predictive values). The sensitivity was 71.4% (20/28) for malignant tumours, 77.8% (7/9) for borderline tumours, and 100% (229/229) for benign tumours. The specificity was 100%, 98.4%, and 83.8% for malignant, borderline, and benign lesions, respectively. The false-positive rate was 0%, false-negative rate was 3.8% (10/266), and concordant report rate was 96.2% (256/266).

The pathology result was higher than the frozen-section result in 3.8% (10/266) cases and lower in 0%.

Discussion

The frozen-section procedure is a widely used diagnostic test because of the insufficiency of pre-operative diagnostic tools such as imaging and tumour markers. Frozen-section examination determines the type and extent of the surgery that will be performed, primarily for ovarian tumours, and therefore directly impacts the morbidity of the patient. The overall accuracy (total concordance between frozen and final diagnosis divided by the total patient number) of frozen section at the diagnosis of ovarian tumours has been reported between 86 and 97% in different studies.^{6,8,13-15} In the present study, the accuracy rate was 96.2%.

In our study, the false-positive rate was 0%. In the literature, the false-positive rate is lower than the false-negative rate; reported false-positives rates range from 2.2 to 10.7%, and false-negative rates, from 5.4 to 29.3%.^{16,17} Sensitivity rates reported in the literature are 98 to 99% for benign and 88.7% for malignant tumoural lesions.¹⁶⁻¹⁸ In a meta-analysis of 18 studies, Geomini et al. found that sensitivity ranged from 65 to 97% for benign and from 71% to 100% for malignant lesions, and specificity ranged from 97 to 100% for benign and from 98.3 to 100% for malignant lesions.⁶ Results from the present study were similar to those of this meta-analysis, except that we found a lower specificity for benign tumours (83.8%).

The definitive histopathological result of benign frozen section diagnosis as borderline and borderline frozen section diagnosis as malignant can be expected. However, definitive histopathological result of benign frozen section diagnosis as malignant is the most unwilling result.

In our study, inadequate and inappropriate tissue sampling during operation and frozen section due to huge tumours, and limited number of sections and for the pathologist to be poorly — informed about clinical features of the patient and findings during operation were the reasons for the cases with benign frozen but borderline paraffin-block results and borderline frozen but malignant paraffin-block results. In addition to these, difficulties during evaluation of the histopathological features especially for malignant mesenchymal tumour, signet ring cell carcinoma of stomach

(Krukenberg tumour) and granulosa cell tumours (two cases) were the reasons for misdiagnosis for the cases that had benign frozen but malignant paraffin-block results in our study. The experience of the pathologist also affected our results.

For the diagnosis of borderline tumours, sensitivity was higher (77.8%) in the present study than that in previous studies (44-64%).¹⁶⁻¹⁹ This may be explained by the lower number of borderline tumours and the poor positive predictive value. When borderline tumours are compared with malignant tumours, the sensitivity of the test is higher; however, the positive predictive value is lower in borderline than in malignant tumours.

Misdiagnosis of borderline tumours may be related to several factors: tumour size, histologic type, and pathologist's experience. Geomini et al. found that the likelihood ratio of a benign frozen-section diagnosis in the presence of malignancy was higher when the tumour size was larger than 10 cm.²⁰ Additionally, Tempfer et al. reported tumour size as a sole predictive factor in the underdiagnosis of borderline tumours.¹² Conversely, in one study, a tumour size of less than 10 cm was found to be a predictor of misdiagnosis in borderline tumours.²¹ In that study, Brun et al. found that tumour size and mucinous type were the main factors associated with misdiagnosis of borderline tumours.

The larger tumour size and multilocular pattern of mucinous tumours is reported to have a negative effect on the accuracy of frozen-section diagnosis.^{2-4,8,18,22-23} Mucinous tumours can comprise benign, borderline, and malignant components simultaneously. Multivariate analysis found that the mucinous type was the only independent factor in the misdiagnosis of borderline neoplasms.¹⁷ Some authors have suggested that underdiagnosis was due to sampling errors, and they advised using greater numbers of frozen sections to minimise the underdiagnosis of tumours, recommending one section per 10 cm of the mass.^{4,24} Some recent studies have indicated that after sampling errors, the absence of an expert pathologist is responsible for the misdiagnosis of tumours.^{21,22} In contrast to these studies, however, Menzin et al. found no correlation between pathologist and frozen-section misdiagnoses.²⁵ In addition, pathologists should be informed about tumour status, peritoneal implants, and the contralateral ovary. Because of this, some surgeons prefer the term "intra-operative consultation" to "frozen-section examination."¹⁰

Conclusion

Frozen-section examination is a method with adequate sensitivity and specificity. It has low false-positive and -negative rates. It can be safely used to guide the intraoperative management of ovarian masses.

References

- Spann CO, Kennedy JE, Musoke E. Intraoperative consultation of ovarian neoplasms. *J Natl Med Assoc* 1994; 86: 141-4.
- Twaalfhoven FC, Peters AA, Trimbos JB, Hermans J, Fleuren GJ. The accuracy of frozen section diagnosis of ovarian tumors. *Gynecol Oncol* 1991; 41:189-92.
- Pinto PB, Andrade LA, Derchain SF. Accuracy of intraoperative frozen section diagnosis of ovarian tumors. *Gynecol Oncol* 2001; 81: 230-2.
- Wang KG, Chen TC, Wang TY, Yang YC, Su TH. Accuracy of frozen section diagnosis in gynecology. *Gynecol Oncol* 1998; 70: 105-10.
- Michael CW, Lawrence DW, Bedrossian CWM, F.I.A.C. Intraoperative consultation in ovarian lesions: a comparison between cytology and frozen section. *Diagnostic Cytopathology* 1996; 15: 387-94.
- Geomini P, Bremer G, Kruitwagen R, Mol BW. Diagnostic accuracy of frozen section diagnosis of the adnexal mass: a metaanalysis. *Gynecol Oncol* 2005; 96: 1-9.
- Boriboonthirunsam D, Semboon A. Accuracy of frozen section in the diagnosis of malignant ovarian tumor. *J Obstet Gynaecol Res* 2004; 30: 394-9.
- Baker P, Oliva E. A Practical approach to intraoperative consultation in gynecological pathology. *Int J Gynecol Pathol* 2008; 27: 353-65.
- Wakahara F, Kikkawa F, Nawa A, Tamakoshi K, Ino K, Maeda O et al. Diagnostic efficacy of tumor markers, sonography, and intraoperative frozen section for ovarian tumors. *Gynecol Obstet Invest* 2001; 52: 147-52.
- Ilvan S, Ramazanoglu R, Ulker Akyildiz E, Calay Z, Besse T, Oruc N. The accuracy of frozen section (intraoperative consultation) in the diagnosis of ovarian masses. *Gynecol Oncol* 2005; 97: 395-9.
- Wootipoom V, Dechsukhum C, Hanprasertpong J, Lim A. Accuracy of ?intraoperative frozen section in diagnosis of ovarian tumors. *J Med Assoc Thai* 2006; 86: 577-81.
- Tempfer CB, Polterauer S, Bentz E, Reinthaller A, HeXer LA. Accuracy of intraoperative frozen section analysis in borderline tumors of the ovary: a retrospective analysis of 96 cases and review of the literature. *Gynecol Oncol* 2007; 107: 248-52.
- Acs G. Intraoperative consultation in gynaecologic pathology. *Semin Diagn Pathol* 2002; 19: 237-54.
- Medeiros LR, Rosa DD, Edelweiss MI, Stein AT, Bozzetti MC, Zelmanowicz A, et al. Accuracy of frozen-section analysis in the diagnosis of ovarian tumors: a systematic quantitative review. *Int J Gynecol Cancer* 2005; 15: 192-202.
- Rakhshan A, Zham H, Kazempour M. Accuracy of frozen section diagnosis in ovarian masses: experience at a tertiary oncology center. *Arch Gynecol Obstet* 2009; 280: 223-8.
- Gol M, Baloglu A, Yigit S, Dogan M, Aydin C, Yensel U. Accuracy of frozen section diagnosis in ovarian tumors: Is there a change in the course of time? *Int J Gynecol Cancer* 2003; 13: 593-7.
- Houck K, Nikrui N, Duska L, Chang Y, Fuller AF, Bell D, et al. Borderline tumors of the ovary: correlation of frozen and permanent histopathologic diagnosis. *Obstet Gynecol* 2000; 95: 839-43.
- Tangjitgamol S, Jesadapatrakul S, Manusirivithaya S, Sheanakul C. Accuracy of frozen section in diagnosis of ovarian mass. *Int J Gynecol Cancer* 2004; 14: 212-9.
- Maheshwari A, Gupta S, Kane S, Kulkarni Y, Goyal BK, Tongaonkar HB. Accuracy of intraoperative frozen section in the diagnosis of ovarian neoplasms: experience at a tertiary oncology center. *World J Surg Oncol* 2006; 4:12.
- Geomini PM, Zuurenok LD, Bremer GL, deGraaff J, Kruitwagen RF, Mol BW. The impact of size of the adnexal mass on the accuracy of frozen section diagnosis. *Gynecol Oncol* 2005; 99: 362-66.
- Brun JL, Cortez A, Rouzier R, Callard P, Bazot M, Uzan S, et al. Factors influencing the use and accuracy of frozen section diagnosis of epithelial ovarian tumors. *Am J Obstet Gynecol* 2008; 199: 244.e1-7.
- Stewart CJ, Brennan BA, Hammond IG, Leung YC, McCartney AJ. Intraoperative assessment of ovarian tumors: a 5-year review with assessment of discrepant diagnostic cases. *Int J Gynecol Pathol* 2006; 25: 216-22.
- Yarandi F, Eftekhari Z, Izadi-Mood N, Shojaei H. Accuracy of intraoperative frozen section in the diagnosis of ovarian tumors. *Aust N Z J Obstet Gynaecol* 2008; 48: 438-41.
- Obiakor I, Maiman M, Mittal K, Awobuluyi M, DiMaio T, Demopoulos R. The accuracy of frozen section in the diagnosis of ovarian neoplasms. *Gynecol Oncol* 1991; 43: 61-3.
- Menzin AW, Rubin SC, Noumo V JS, Livolsi VA. The accuracy of a frozen section diagnosis of borderline ovarian malignancy. *Gynecol Oncol* 1995; 59: 183-5.